Multiscale Modeling of Clotting Risk in Atrial Fibrillation

Boyce Griffith, Simone Rossi, Margaret Anne Smith, and John Vavalle, UNC
Craig Henriquez, Tristram Bahnson, and Stephen Gaeta, Duke University
Aaron Fogelson, University of Utah
boyceg@email.unc.edu ch@duke.edu fogelson@math.utah.edu

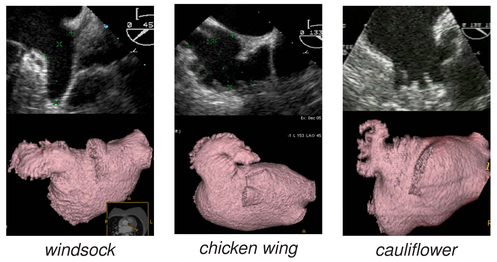
Overview

Atrial fibrillation (AF) is the most common sustained arrhythmia in the U.S. Complications include thromboembolism and stroke.

Anticoagulation is commonly prescribed to patients with elevated stroke risk. Current risk assessment indices lack individualization and classify most AF patients as being at *intermediate risk*.

The *long-term objective* of this research is to develop broad-spectrum approaches to clotting risk assessment in AF that provide personalized risk prediction.

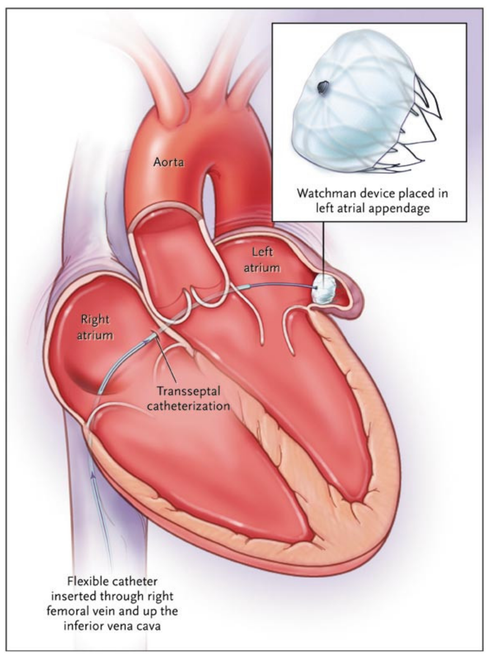
The *specific aims* of this project focus on constructing, verifying, and validating comprehensive models of atrial dysfunction to enable mechanistic studies of flow and clotting in AF.



windsock *chicken wing* *cauliflower*

Typical LAA morphologies. *Top:* echo. *Bottom:* CT.

In AF, most clinically significant thrombi form in the **left atrial appendage (LAA)**. Initial work is focused on developing models of flow and clotting in the LAA.



Percutaneous LAA closure via *WATCHMAN*. (From W. H. Maisel, *N Engl J Med* 360:2601–2603, 2009.)

Model Components

We aim to simulate the impacts on flow and clotting risk of specific interventions:

- *percutaneous LAA exclusion*
- *catheter ablation therapy for AF*

These require models that couple

- electrophysiology
- muscle mechanics
- fluid dynamics
- thrombogenesis

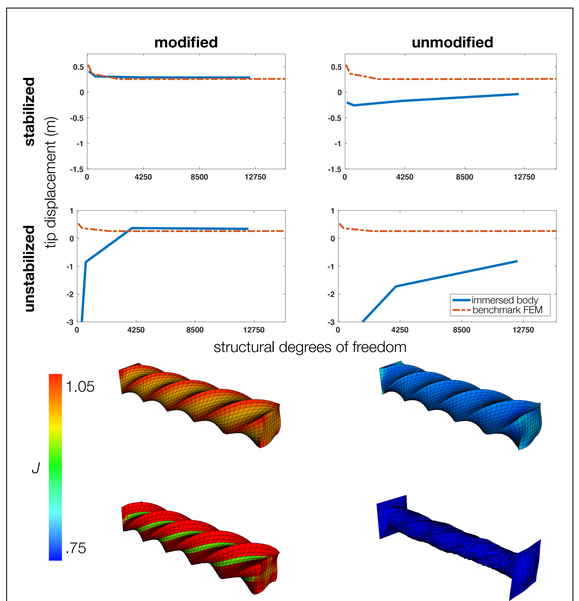
in subject-specific anatomical models.

Simulation methods include:

- **computational fluid dynamics** by AMR finite volume methods for the incompressible Navier-Stokes equations
- **computational solid dynamics** by stabilized mixed finite element methods for incompressible and nearly incompressible nonlinear elasticity
- **fluid-structure interaction** by AMR immersed boundary (IB) methods
- **electrophysiology** by AMR finite element methods
- **thrombogenesis** via finite volume methods for reaction-advection-diffusion equations

Verification

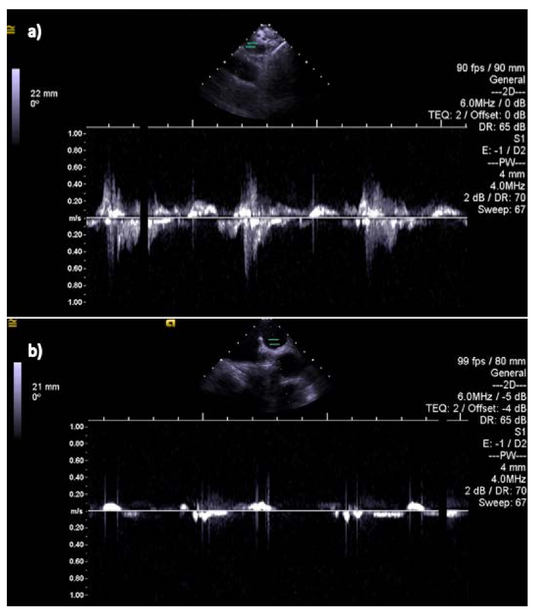
Verification will use benchmark problems with known analytic solutions or with consensus solutions.



Nonlinear elastic beam torsion test to verify solution accuracy of FSI methods.

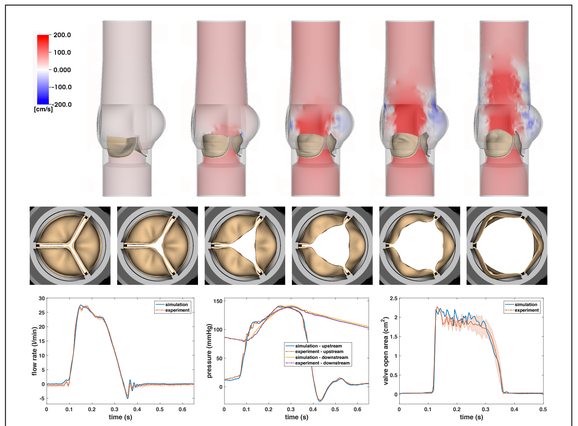
Model Credibility Plan

1. **Context:** Atrial dynamics in normal sinus rhythm and in atrial fibrillation.
2. **Data:** In vivo and in vitro data relevant to cardiac fluid dynamics, muscle mechanics, electrophysiology, and thrombosis at the organ scale.
3. **Evaluation:** Against benchmark data. We shall compare velocities (of the flow, muscle, and electrical activation), deformations, and stresses.
4. **Limitations:** Established by benchmarking and uncertainty quantification.
5. **Version control:** `git` is used for software and model repositories.
6. **Document:** Simulation infrastructure is documented through `ibamr.github.io`. Documentation is generated through in-line comments processed by Doxygen (`www.doxygen.nl`) and documentation is generated automatically by Travis CI (`travis-ci.org`).
7. **Dissemination:** Simulation infrastructure is distributed through *GitHub*. The project plans to use *GitHub* to distribute model data as feasible.
8. **Review:** In vitro models of cardiac flow are are expected to be submitted to the FDA *Medical Device Development Tools* program as non-clinical assessment models.
9. **Competing implementations:** Where possible, we use community tests to compare against alternative methods and implementations.
10. **Standards:** Software will be tested using a variety of compilers using a dedicated Jenkins CI server (`jenkins.io`). Models will use standard formats for organ-scale model specification as such formats emerge.

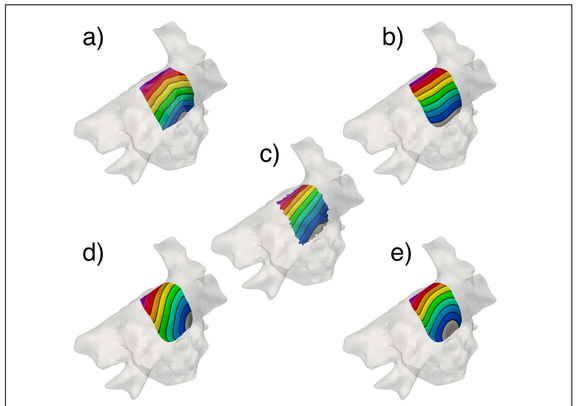


Pulsewave Doppler data from a) the LAA ostium a patient showing normal flow and b) the LAA remnant of a patient with prior surgical ablation (maze) and occlusion of the LAA showing low flow.

Initial Validation

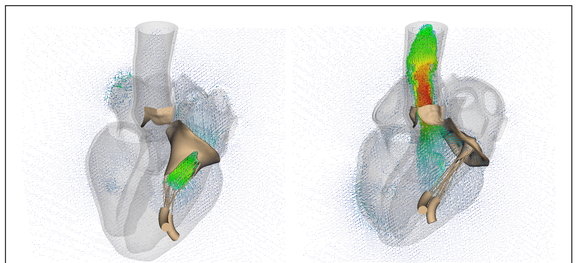


Validation of FSI models of cardiac valve dynamics in a pulse duplicator. *Top:* Simulated flow along the aortic test section. *Middle:* Simulated leaflet opening dynamics. *Bottom:* Comparison of computational and experimental flow dynamics and leaflet kinematics.



Computational and clinical activation times along the LA posterior wall. a,b,d,e) Simulations with different fiber orientations and pacing sites. c) Clinical activation times from a surround flow catheter.

Model Results



Initial results from a subject-specific FSI heart model. *Left:* atrial systole. *Right:* ventricular systole.

Acknowledgements

Thanks to BA Craven, EM Kolahdouz, JH Lee, C Puelz, LN Scotten, and DR Wells. Funding from NIH U01HL143336, NSF CBET 1757193, OAC 1450327, OAC 1652541.